

**IN THE CLAIMS**

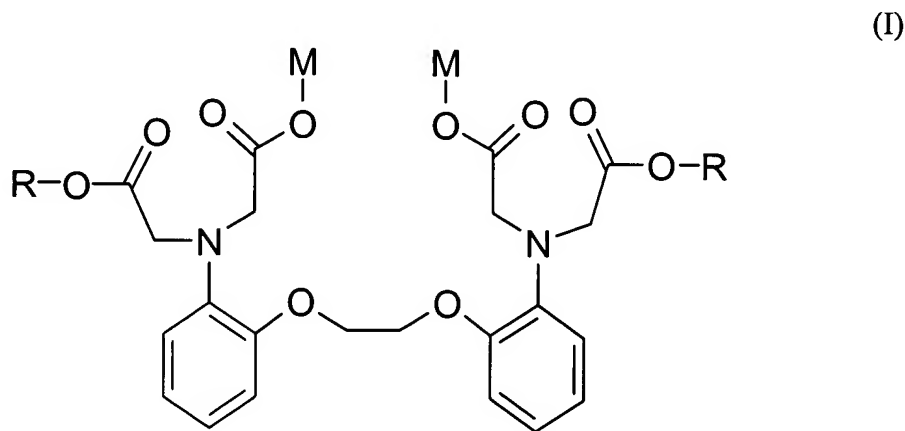
Please amend claims 2, 9, 11-15, 17, 19, 21, 23, 26, 28 and 30 as indicated below.

Please cancel claims 3, 4, 10, 16, 24, 25, and 29 as indicated below.

This listing of claims below will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Original) A method of inhibiting protease activity, said protease being selected from metalloproteinase and calpain, the method comprising exposing cells to inhibiting amount of a compound of the general formula (I):



wherein

R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any combination of 1-6 oxygen and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other; and

M denotes a hydrogen or a physiologically acceptable cation.

2. (Currently Amended) The method according to claim 1 wherein R is a phenylalkyl, an alkyl interrupted by zero to three oxygen atoms, or a monoalkyl ether of mono-, di-, or tri-ethylene glycol.

3-4. (Canceled)

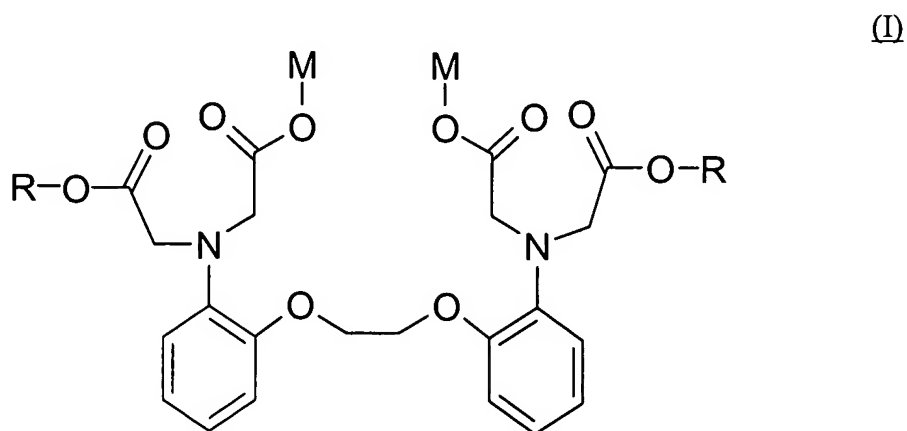
5. (Original) The method according to claim 1 wherein R is selected from the group consisting of:  $C_8H_{17}$ ,  $C_8H_{17}OCH_2CH_2$ ,  $C_{18}H_{37}$ ,  $C_{18}H_{37}OCH_2CH_2$ , benzyl- $CH_2OCH_2CH_2$ ,  $C_{12}H_{25}OCH_2CH_2$ ,  $C_{12}H_{25}(OCH_2CH_2)_2$  and  $C_{12}H_{25}(OCH_2CH_2)_3$ .

6. (Original) The method according to claim 1, wherein said protease is a matrix metalloproteinase (MMP).

7. (Currently Amended) The method according to claim 6 1, wherein ~~the matrix~~ said metalloproteinase is MMP-9.

8. (Original) The method according to claim 1, wherein said protease is a calpain.

9. (Currently Amended) A method for preventing, treating or managing a MMP-related disease or disorder or a caplain-related disease or disorder in a mammal comprising administering to a mammal in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of a compound of the general Formula (I):



wherein

R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any combination of 1-6 oxygen

and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other; and

M denotes a hydrogen or a physiologically acceptable cation.

10. (Canceled)

11. (Currently Amended) The method according to claim 9 ~~or 10~~, wherein said method further comprises treating the mammal with additional therapeutic treatment.

12. (Currently Amended) The method according to claim ~~any one of claims 9 to 11~~, wherein said mammal is a human.

13. (Currently Amended) The method according to claim 9 ~~or 10~~, wherein said MMP- or calpain-related disease or disorder is selected from the group consisting of cancer, stroke, trauma, inflammatory conditions and diseases, atherosclerosis, thrombotic disorders, arthritis, hemorrhage, rheumatic diseases, autoimmune diseases, neurological diseases and disorders, migraine, cerebrovascular and cardiovascular disorders.

14. (Currently Amended) The method according to claim 9 ~~13~~, wherein said MMP- or caplain-related disease or disorder is an inflammatory condition or disease ~~conditions and diseases are~~ selected from the group consisting of arthritides, rheumatoid arthritis, osteoarthritis, restenosis, asthma, psoriasis, systemic lupus erythematosus, inflammatory bowel syndrome, Crohn's disease, migraine, gingivitis, periodontitis, meningitis, tropical spastic paraparesis, sepsis, bullous skin disorders, acne and inflammation due to infectious diseases.

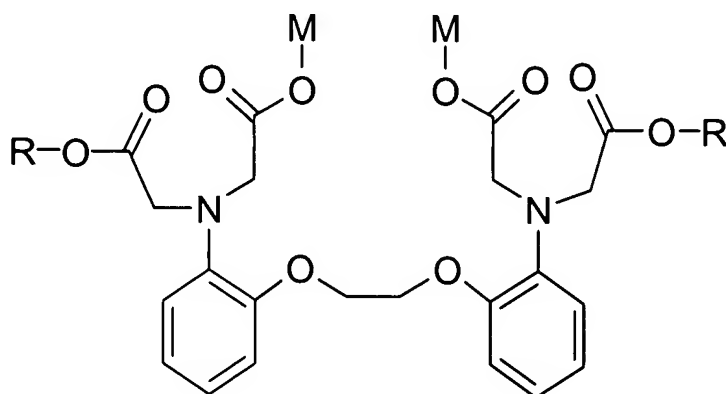
15. (Currently Amended) The method according to claim 9 ~~or 10~~, wherein said MMP- or calpain-related disease or disorder is selected from the group consisting of ischemic or hypoxic tissue damage, oxidative damage, osteoporosis, diabetes, hemorrhage, ocular pathologies and retinopathies, diabetic retinopathy, glaucoma, macular degeneration, cataract, retinal detachment and retinal tears or neurodegenerative diseases or disorders, multiple sclerosis (MS), Alzheimer's disease (AD), motor neuron disease (MND), amyotrophic lateral sclerosis (ALS), Guillain-Barré,

Parkinson's disease, Huntington disease, Pick's disease, dementia syndrome, vascular dementia, multiple infarct dementia, HIV-induced neural disorders, brain ischemia (both global and focal ischemia) and neuronal tissue trauma.

16. (Canceled)

17. (Currently Amended) A method for preventing, treating or managing cancer associated with increased activity of metalloproteinase comprising administering to a patient in need thereof a pharmaceutical composition comprising a therapeutically effective amount of a compound of the general Formula (I):

(I)



wherein

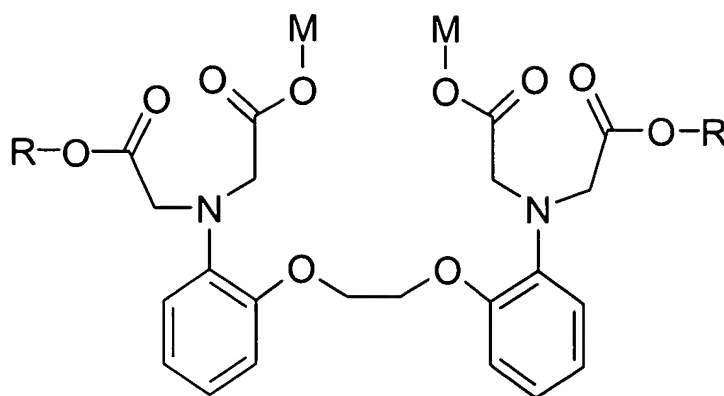
R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any combination of 1-6 oxygen and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other; and

M denotes a hydrogen or a physiologically acceptable cation.

18. (Original) A method according to claim 17, wherein said cancer includes cancer metastasis.

19. (Currently Amended) A method for treating a patient suffering from an angiogenesis-dependent disease comprising administering to said patient a pharmaceutically effective amount of a compound of the general Formula (I):

(I)



wherein

R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any combination of 1-6 oxygen and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other; and

M denotes a hydrogen or a physiologically acceptable cation.

20. (Original) The method according to claim 19, wherein said angiogenesis-dependent disease is selected from cancerous tumors, arthritis, psoriasis, macular degeneration, chronic inflammation and diabetic retinopathy.

21. (Currently Amended) The method according to claim 17 ~~any one of claims 17 to 19~~, wherein said method further comprises treating the patient with additional therapeutic treatment.

22. (Original) The method according to claim 21, wherein said additional treatment is selected from chemotherapy, irradiation therapy, immunotherapy, genetic therapy and surgery.

23. (Currently Amended) The method according to claim ~~19~~ 21, wherein said method further comprises treating the patient with additional therapeutic treatment ~~additional treatment is carried out concurrently with the administration of the pharmaceutical composition comprising a compound of the general Formula (I).~~

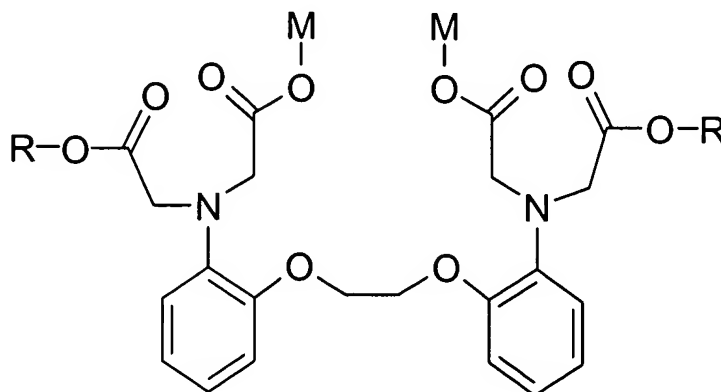
24-25. (Canceled)

26. (Currently Amended) The method according to claim 9 ~~any one of claims 9 to 25~~, wherein said compound of the general formula I is selected from the group consisting of

1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octoxyethyl acetate), N,N'-diacetic acid;  
 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octodecyloxyethyl acetate), N,N'-diacetic acid;  
 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-benzyloxyethyl acetate), N,N'-acetic acid;  
 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-dodecyloxyethyl acetate), N,N'-diacetic acid;  
 1,2-bis(2-aminophenoxy)ethane, N,N'-di[2-(2-dodecyloxyethoxy)-ethyl acetate], N,N'-diacetic acid; and  
 1,2-bis(2-aminophenoxy)ethane, N,N'-di {2-[2-(2-dodecyloxyethoxy)ethoxy]-ethyl acetate}, N,N'-diacetic acid.

27. (Currently Amended) A method for the preparation of a medicament for inhibiting the activity of a protease selected from metalloproteinase and calpain which comprises utilizing Use of a compound of the general formula (I):

(I)



wherein

R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any combination of 1-6 oxygen and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other; and

M denotes a hydrogen or a physiologically acceptable cation;

~~for the preparation of a medicament for inhibiting the activity of a protease selected from metalloproteinase and calpain.~~

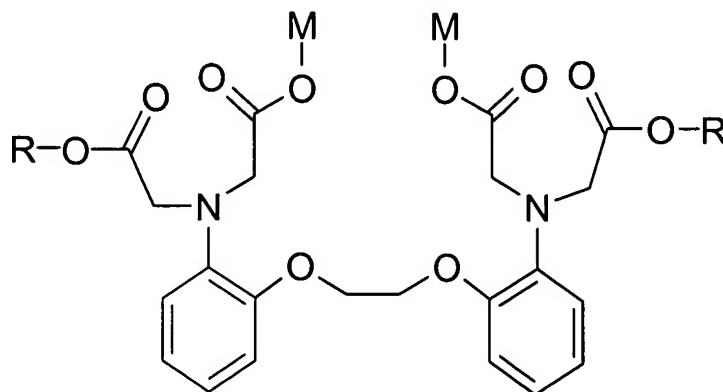
28. (Currently Amended) The method use according to claim 27, wherein said compound of the general formula (I) is selected from the group consisting of

- 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octoxyethyl acetate), N,N'-diacetic acid;
- 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-octodecyloxyethyl acetate), N,N'-diacetic acid;
- 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-benzyloxyethyl acetate), N,N'-acetic acid;
- 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-dodecyloxyethyl acetate), N,N'-diacetic acid;
- 1,2-bis(2-aminophenoxy)ethane, N,N'-di[2-(2-dodecyloxyethoxy)-ethyl acetate], N,N'-diacetic acid; and
- 1,2-bis(2-aminophenoxy)ethane, N,N'-di{2-[2-(2-dodecyloxyethoxy)ethoxy]-ethyl acetate}, N,N'-diacetic acid.

29. (Canceled)

30. (Currently Amended) A compound of the general formula (I):

(I)



wherein

R is saturated or unsaturated alkyl, cycloalkyl, arylalkyl or cycloalkyl-alkyl radical having from 1 to 28 carbon atoms which may be interrupted by any combination of 1-6 oxygen

and/or nitrogen atoms, provided that no two oxygen atoms or an oxygen and a nitrogen atom are directly connected to each other; and

M denotes a hydrogen or a physiologically acceptable cation,

which is 1,2-bis(2-aminophenoxy)ethane, N,N'-di(2-benzyloxyethyl acetate), N,N'-acetic acid.

31. (Original) A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 30 and a pharmaceutically acceptable carrier or excipient.